

REMARKS

Favorable reconsideration of this application in light of the preceding amendments and the following remarks is respectfully requested.

No claims having been added and Claims 4 and 12-15 having been cancelled herein, the Applicants respectfully submit that claims 1-3, 5-11, and 16-24 remain properly under consideration in this Application. Support for amendments to Claim 1 can be found throughout the specification, for example on pages 10, 11, 13 and as shown in Figures 1-3. No new matter has been introduced by the present amendments.

REJECTION UNDER 35 U.S.C. § 112-1ST PARAGRAPH

Claims 1-24 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for “[A] method for generating an ornamental fish comprising (a) generating a transgenic oviparous fish whose genome comprises one or more genes encoding a fluorescent protein operably linked to a promoter, wherein the transgene is expressed in the fish; (b) breeding the transgenic fish with a fish of the same or different species of the same genus having a phenotype or pattern that differs from the transgenic fish; and (c) screening the resulting transgenic progeny of those showing a phenotype or pattern that differs from each parent and fish made by said method”, the specification is alleged not to reasonably provide enablement for the claimed method with a transgenic viviparous fish or for mating fish across genera or family. (Action at pages 2-3). The Action specifically alleges that the “specification does not enable the use of viviparous fish as the method steps differ in scope and fail to limit the species of fish to oviparous species.” This rejection is respectfully traversed.

Applicants respectfully submit that the amendment to Claim 1, specifically reciting "generating a transgenic oviparous fish" obviates the present rejection.

Claims are also allegedly rejected for failing to set forth, of the many families of fish, which species of fish would provide valuable hybrid offspring." (Action at page 4). Specifically, the Action asserts that the specification fails to: "provide the guidance necessary to overcome the unpredictability in the art relating to mating fish of divergent species. It would require undue experimentation to determine successful hybrid species using matings between fish of different genera." (Action at page 4).

Applicants submit that the amendments to the claims reflected above are sufficient to limit the claims to species in the Cyprindae and Killifish groups for which enablement has been provided. Applicants have further cancelled Claims 12-15.

Accordingly, Applicants submit that the amendments to the claims reflected above are sufficient to overcome this rejection.

The Applicants respectfully request therefore, that these rejections under 35 U.S.C. § 112, first paragraph of Claims 1-11, and 16-24 be reconsidered and withdrawn.

REJECTION UNDER 35 U.S.C. § 112-2ND PARAGRAPH

Claims 1-24 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner alleges that Claim 1 remains unclear for failing to recite what is to be screened. This rejection is respectfully traversed.

Applicants submit that the amendments to the claims reflected above are sufficient to provide further clarity by amending Claim 1, step (c) to recite "screening the transgenic progeny

for those exhibiting a phenotype or pattern unlike either parent fish, ..." as recommended by the Examiner. (Action at page 4).

Claim 1 is further rejected under the present rejection for allegedly not providing clarity because "the claim is not clearly limited to making an adult fish as indicated by Applicant at page 9, paragraphs 1 and 2 of Applicant's Remarks dated 10/03/2006." (Action at page 5).

Applicants have overcome this rejection of Claim 1 and dependent claims thereon, by amending Claim 1 to now recite step "(d) growing the transgenic progeny until adult stage." This amendment to step (d) requires an adult fish to be made.

Claim 1 is further alleged to be unclear because "it is not clear if the α -actin or β -actin promoter is part of the claimed transgene or is an endogenous promoter or part of some other exogenous DNA." the genome of the transgenic fish comprises: "a transgene comprising a gene encoding a fluorescent product operably linked to α -actin or β -actin promoter..." The Applicants have overcome this rejection by inserting an amendment as recommended by the Examiner reciting a transgene comprising a gene encoding a fluorescent product operably linked to the promoter.

Claim 23 is allegedly improper for insufficient antecedent basis for the limitation "The ornamental fish" in line 1. The Applicants have hereby amended Claim 23 as suggested by the Examiner to specifically recite "An ornamental fish..."

Accordingly, Applicants submit that the amendments to Claim 1 and claims dependent thereon reflected above are sufficient to overcome this rejection.

The Applicants respectfully request therefore, that the rejections under 35 U.S.C. § 112, second paragraph of Claims 1-11, and 16-24 be reconsidered and withdrawn.

REJECTION UNDER 35 U.S.C. § 102

Claims 1, 2, 5-9, and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Higashijima (Developmental Biology, 1997, 192:289-299). This rejection is respectfully traversed for the reasons detailed below.

At the outset, Applicants appreciate Examiner's withdrawal of the 35 U.S.C. 102(a) rejections of Claims 1, 2, 5-9 and 23 under Lawson and Fadool.

Applicants respectfully submit that Claims 1, 2, 5-9 and 23 are not rendered anticipated by Higashijima et al. (Developmental Biology, 1997, 192:289-299, herein referred to as "Higashijima").

Higashijima teaches that fluorescent germline transmitting zebrafish founders can be made to express GFP using tissue specific promoters β -actin and α -actin promoters. The mosaic expressing founders were mated with wild-type zebrafish to generate F1 progeny that exhibited inherited GFP expression. (Higashijima at page 297, 1st paragraph).

The Applicants maintain that Higashijima fails to teach the limitations of the methods of the presently amended Claim 1 and claims dependent thereon. The presently amended Claim 1 recites a method of producing transgenic oviparous fish using a transgene having flanking inverted terminal repeats operably linked to the fluorescent gene product. Higashijima fails to teach or disclose such a claim limitation.

Moreover, Higashijima fails to teach the breeding step (b) of the presently amended Claim 1, wherein the transgenic fish can be bred with a fish selected from the same or different species with different phenotype or pattern to obtain transgenic progeny.

Since to anticipate a claim, the reference of record must teach every element of the claim, Applicants respectfully submit that Higashijima fails to anticipate Claim 1 and claims dependent thereon, including Claims 2, 5-9 and 23. (MPEP 2131).

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of Claims 1, 2, 5-9 and 23 under 35 U.S.C. § 102(b).

REJECTION UNDER 35 U.S.C. § 103

Claims 1, 2, 5-9, and 23 stand rejected under 35 U.S.C. § 103(a) as being obvious over Higashijima in view of Lawson and Weinstein (Developmental Biology, 248:307-318, of record) herein “Lawson”. This rejection is respectfully traversed.

The Examiner alleges that Higashijima fails to teach breeding the transgenic to fish of a different phenotype or pattern other than that caused by the transgene. The Examiner alleges that the deficiency posed in Higashijima is provided in Lawson (action at page 7). Specifically, the Examiner alleges that Lawson teaches generating a transgenic GFP expressing zebrafish using wild-type, pigmented (EK) *Danio rerio* (*Brachydanio rerio*). Further that the transgenic fish was mated to an unpigmented albino mutant of the same species. (Action at page 7). The Examiner contends that the Albino mutants have an altered body transparent level as a result of a loss of pigmentation. Ultimately, the Examiner contends that it would have been obvious to combine the teachings of Higashijima in making a transgenic fish exhibiting stable and reproducible fluorescent reporter gene expression with those of Larson to mate the transgene of Higashijima into an albino mutant fish.

Applicants respectfully submit that such a combination would not have been motivated after a careful reading of the references. Furthermore, one of ordinary skill in the art would not have an expectation of success without undue experimentation because the genetic constructs of

the two references are distinct and the expression of one construct in one strain of zebrafish using one promoter would not guarantee success in expression of a second strain of zebrafish using a different promoter for expression in a mutant zebrafish.

Applicants respectfully submit that Higashijima's objective in creating such a transgenic fish exhibiting fluorescence is to determine whether tissue specific, in particular non-variegated expression throughout the musculature using zebrafish β -actin promoters (Higashijima at page 290, bottom of col. 1 spanning top of col. 2). On the other hand, Lawson describes the use of the fli1 promoter for vascular expression. (Lawson at page 314). The objective of developing transgenic zebrafish that have EGFP expression in *mib^{ta52b}* mutant albino embryos and adults is to monitor and visualize blood vessel development as it occurs *in vivo*. (Lawson at page 314, col. 2). There is no motivation to combine and mate the transgenic fish of Higashijima to the albino mutant fish of Lawson (*mib^{ta52b}*), because the albino mutant fish of Lawson have a variety of vascular defects as a result of Notch signaling loss. (Lawson at page 316, col. 1, spanning to top of col. 2). The resultant progeny of such crosses would not be conducive to successful ornamental fluorescent fish for commercial purposes.

Furthermore, neither Higashijima, nor Lawson recite the claim limitation "breeding the transgenic oviparous fish with a fish selected from the same or different species with different phenotype or pattern" as found in the presently amended Claim 1.

Applicants provide a table to summarize the references of record and the present exemplified embodiments to distinguish the various characteristics.

Table 1: Comparison between the present invention and previous revealed techniques

	The present invention	Higashijima	Lawson
Transgenic GFP zebrafish	V	V	V
Promoter	α -actin; β -actin	α -actin; β -actin	fli1
Inter-specific breeding	V	X	X
Fluorescent gene expressed throughout the body	V	V	X
Ornament	V	X	X
Adult fish	V	V	X

Accordingly, Applicants submit that Higashijima in view of Lawson fails to render Claim 1 and dependent Claims 2, 5-9, and 23 obvious.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of Claims 1, 2, 5-9 and 23 under 35 U.S.C. § 103(a).

Claim 4 stands rejected under 35 U.S.C. § 103(a) as being obvious over Higashijima (*Developmental Biology*, 1997, 192:289-299) in view of Bartley et al. (*Reviews in Fish Biology and Fisheries*, 2001, 10:325-337) taken with Gong et al. (*Genetica*, 111:213-225, 2001). This rejection is respectfully traversed.

Applicants respectfully submit that the presently amended claims, including the cancellation of Claim 4 herein, render this rejection moot.

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Application No. 10/791,536
Attorney Docket No. 8964-000010/US

Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Double patenting

Examiner submits that if Claim 3 were found allowable, claim 4 would be objected to under 37 CFR 1.75, as being a substantial duplicate thereof. (Action at page 9). The Applicant submits that the cancellation of Claim 4 is sufficient to overcome and/or render this Double Patenting objection moot.

CONCLUSION

In view of the above elections, the Applicant submits that the present application is in condition for allowance. A notice to that effect is respectfully requested.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned. If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge any underpayment or non-payment of any fees required under 37 C.F.R. §§ 1.16 or 1.17, or credit any overpayment of such fees, to Deposit Account No. 08-0750, including, in particular, extension of time fees.

Respectfully submitted,

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